



Preeclampsia-eclampsia as a risk factor for the development of chronic kidney disease: A 11 years single-center observational study

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Abstract

Introduction: Preeclampsia-eclampsia is a prevalent systemic disorder of pregnancy characterized by various manifestations of organic dysfunction, mainly hypertension, and proteinuria, a sign of renal dysfunction. Little is known about its long-term effects on the kidney, either in terms of physical damage as measured by albuminuria or proteinuria, development of chronic arterial hypertension, functional impairment as measured by reduced glomerular filtration rate, or terminal renal failure.

Methods: The present study is observational, analytical, and retrospective. Data were taken from the medical records of patients with a history of preeclampsia-eclampsia treated in the gynecology and obstetrics service of the Hospital de Especialidades Carlos Andrade Marín diagnosed from January 2008 to December 2018 (exposed group) and healthy pregnant women during the period. During the same period (non-exposed group), once randomized, follow-up is performed to establish the prevalence of some degree of chronic kidney disease in the groups.

Results: The sample consists of 402 women; 201 correspond to the exposed group and 201 to the control group. Women with a history of preeclampsia-eclampsia had a higher risk of developing CKD with a RR of 3.3 (95% CI: 1.67-6.51).

Conclusions: Women with a history of preeclampsia-eclampsia in their pregnancies had a higher risk of developing any degree of CKD in the future.

Keywords:

MESH: Eclampsia; Pre-Eclampsia; Renal Insufficiency, Chronic; Proteinuria; Hypertension; Hematuria.

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D Among the different pathologies associated with pregnancy, hypertensive disorders are the most prevalent, with preeclampsia being the most common form. The preeclampsia (PE) rate varies between 5% and 10% in developed countries; this figure could be increased to 18% in some developing countries [1].

This pathology occurs concomitantly with reversible renal alterations such as acute renal failure, whose recovery usually occurs within 6 weeks after delivery; however, relatively little is known about long-term effects on the kidney either in terms of physical damage as measured by albuminuria or proteinuria, impaired function as measured by reduced glomerular filtration rate (GFR), or end-stage renal failure [2].

The most frequent cause of acute kidney injury in pregnancy is that associated with preeclampsia-eclampsia; even though in Latin America, there are few data, reports establish that approximately 57% of pregnant women with AKI corresponded to those who presented hypertensive disorders such as preeclampsia, with a maternal mortality of less than 2% [3, 4]. The development of an episode of AKI is associated with a substantial and significant risk of development and progression of end-stage chronic kidney disease (CKD) and even chronic dialysis [5]. Another of the possible long-term implications of preeclampsia-eclampsia at the renal level is that of presenting chronic damage per se to the history of preeclampsia as well; CKD is defined as "kidney damage for at least three months, defined by structural or functional abnormalities of the kidney with or without decreased glomerular filtration rate" [6].

Despite the normalization after delivery of all the maternal alterations developed by preeclampsia, these alterations have not been sufficiently studied due to the widely extended paradigm that the "cure" for preeclampsia-eclampsia is delivery; however, studies consistently show that formerly preeclamptic women experience an approximately doubled risk of cardiovascular events occurring primarily in the fifth and sixth decades of life [7]. In addition, it has been seen that these women develop chronic hypertension 6 to 8 years earlier compared to women with a history of normotensive pregnancy; regarding renal function, there is evidence that it could increase the risk of developing chronic kidney damage [8]; however, there are inconclusive studies such as the study by "Mannist et al." which showed a risk ratio (HR) for the development of CKD after pregnancy-induced hypertension of (HR 1.91) but not after preeclampsia (HR 0.75) [4]. Another study demonstrated the opposite in a retrospective panel of women with a history of preeclampsia with a relative risk (RR) of 4.7 for developing ESRD after correction for traditional risk factors. This risk has been seen to triple when women have more than one pregnancy with preeclampsia [9]. The objective of the present study was to

determine the risk of developing ESRD in a group of pregnant women with pre- and eclampsia compared with a control group with 11 years of follow-up.

Materials and methods

Study design

This study is an observational, case-control, retrospective study.

Scenery

The study was carried out in the Department of Statistics, Obstetrics, and Gynecology and Nephrology of the Hospital de Especialidades "Carlos Andrade Marín," of the Ecuadorian Institute of Social Security in Quito-Ecuador, from January 1, 2021, to September 30, 2021. The retrospective analysis period corresponded to 11 years: from January 1, 2008, to December 31, 2018.

Participants

Pregnant women were included. In the case group, patients with a diagnosis of preeclampsia and eclampsia were registered. Pregnant women were registered in the same period without pathologies in the control group. Cases with a history of chronic and acute kidney disease, patients with a history of chronic and pregestational hypertension, patients with a history of diabetes mellitus types 1 and 2, patients with a history of preexisting heart disease, and patients with a diagnosis of any disease were excluded. This predisposes patients to the development of kidney disease (such as diabetes). Cases with incomplete data for analysis, incomplete medical records, or without postpartum follow-up for at least one year were eliminated.

Variables

The variables were demographic, such as age, ethnicity, education, and parity. Clinical variables: estimated glomerular filtration rate by CKD-EPI, proteinuria, hematuria.

Data sources/measurements

The source was indirect; the institutional electronic file was reviewed, and the registry of the gynecology-obstetrics services was reviewed. Laboratory results were obtained from the electronic laboratory record. The diagnosis of preeclampsia was established with the clinical criteria of present hypertension >140/90 mmHg, proteinuria >300 mg/24 h, thrombocytopenia <150,000/u, liver disease with LDH >600 IU/L, and AST or ALT >70 IU/L. Vasomotor symptoms present: headache, epigastric pain, tinnitus, or scotomata. Eclampsia was established with clinical criteria for seizures in patients with preeclampsia. Kidney disease was classified into five stages according to the glomerular filtration rate. Proteinuria was declared positive



when the concentration was more significant than 150 mg/24 hours or the dipstick gave 1+.

Biases

To avoid possible interviewer, information, and memory biases, the principal investigator guarded the data at all times with a guide and records approved in the research protocol. Observation and selection bias were avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the period above were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

Studio size

The sample was probabilistic; the formula was used: $n=2p^*q(z\alpha +z\beta) 2/(p1-p0) ^2$, with an alpha error of 0.05, a confidence level of 95%, $z\alpha= 1.96$, $z\beta= 0.842$, $p0 = 0.10$, $p1 = 0.2$, and the sample size was 200 cases and 200 controls.

Quantitative variables

Descriptive statistics were used. Scaled results are expressed as means and standard deviations. Categorical data, such as sex, are presented as proportions.

Statistical analysis

Inferential statistics are used. The chi-square test was used to demonstrate a relationship between the variables. The relative risk (RR) was used with the 95% confidence interval and the P value to determine the degree of association. The statistical package used was SPSS 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Results

Participants

A total of 402 patients, 201 cases, and 201 controls were included in the study.

Baseline characteristics of the study population

The characteristics of the population are presented in Table 1. There were no population differences concerning age, ethnicity, education, or parity at the beginning of the study.

Development of kidney disease

At the follow-up visits, the presence of chronic kidney disease was recorded in 35/201 cases (17.41%) versus 10/201 controls (4.98%) ($P<0.001$). The time elapsed between the diagnosis of preeclampsia/eclampsia and the development of CKD was 3.95 years, the minimum time was 3.21 years, and the maximum was 4.7 years (95% CI). The development of CKD in the mestizo ethnic group (Hispanic) was analyzed as a risk factor (Table 2).

Secondary analyses

Logistic regression was used to determine the probability of CKD occurring based on previously analyzed variables with statistical significance, where a history of preeclampsia was ratified with a B value of 1.27; $P= 0.001$ (95% CI 1.689 – 7.55) as a predictor of CKD (Table 3).

Table 1. Descriptive variables of the study

Variable	Cases n=201	Controls n=201	P
Scholarship			
Age (years)	29.5 ± 6.8	31.4 ± 6.5	0.30
ethnicity			
Indigenous	1 (0.5%)	1 (0.5%)	0.90
Hispanic	191 (95.0%)	196 (97.5%)	
Afro-Ecuadorian	9 (4.5%)	4 (2.0%)	
Scholarship			
Primary	24 (11.9%)	29 (14.4%)	0.9105
Secondary	84 (41.8%)	78 (38.8%)	
Higher	93 (46.3%)	94 (46.8%)	
Parity			
Primigravida	57 (28.4%)	53 (26.4%)	0.654
Multigesta	144 (71.6%)	148 (73.6%)	

Table 2. Histopathological diagnoses in the study group.

Variable	Cases n=201	Controls n=201	OR	CI 95%	P
CKD (Stage 1-5)	35 (17.41%)	10 (4.98%)	3,725	1935 – 8381	0.0002
CKD (Stage 5)	6 (2.98%)	0 (0%)	1,764	0.750 – 239.46	0.077
mestizo ethnicity	34 (16.92%)	8 (3.98%)	3,911	2,212 – 10,905	0.0001
Higher Education Vs. Secondary or Primary Education	17 (1.99%)	6 (1.49%)	2,376	1,231 – 8,741	0.0175
Development of arterial hypertension	17 (8.46%)	7 (3.48%)	2,041	1,038 – 6,317	0.0413
Development of proteinuria	12 (5.97%)	3 (1.49%)	2,193	1,164 – 15,083	0.0283
development of hematuria	1 (0.48%)	0 (0%)	0.675	0.122 – 74.456	0.500

CKD: Chronic Kidney Disease

**Table 3.** Variables in the equation in logistic regression

	B.	Standard error	Wald	gl	Next.	Exp(B)	95% IC for Exp (B) lower	95% IC for Exp (B) Higher
Preeclampsia(1)	1,276	0.381	11,233	1	0.001	3,582	1,698	7,552
Multigesta(1)	0.037	0.396	0.009	1	0.925	1,038	0.478	2,255
Age	0.016	0.028	0.318	1	0.573	1,016	0.962	1,072
ethnicity	-	-	1,296	two	0.523	-	-	-
Ethnicity(1)	-19,785	27509.106	0.000	1	0.999	0.000	0.000	-
Ethnicity(2)	-0.804	0.706	1,296	1	0.255	0.448	0.112	1,786
Constant	-2,655	1,041	6,501	1	0.011	0.070	-	-

Discussion

The history of PE has been studied as a risk factor for the development of CKD; in this context, the main results in our study were the following: The incidence of preeclampsia is identified between 5 and 10%, figures that can be considered relatively low; however, in some countries, it is the leading cause of maternal-fetal and perinatal death, despite being identified as priority care [1, 10]. The association between preeclampsia and CKD is high, as revealed by the estimated odds ratio. Despite this association, it cannot be stated that preeclampsia is a risk factor for CKD with the weight indicated by the impossibility of many studies to control all the variables that could intervene in the future development of CKD [10-12].

We seek to answer the question about the risk relationship between a history of preeclampsia and the development of CKD. This association has been investigated for some years in patients with CKD and is the source of continuous work [10, 13].

In recent studies, a history of PE has been associated with a risk factor for the development of CKD [14]; currently, this association is considered an object of observation for personalized follow-up and determination of potentially controllable risk factors in the development of CKD. In the present study, the prevalence of CKD attributable to a history of preeclampsia was 17.41%, similar to previous results [10-12].

The main objective of the study is to demonstrate the association between a history of PE and the development of CKD; in addition, a broader definition of CKD was incorporated using proteinuria, hematuria, and eGFR as determinants of CKD, similar to the previously published study [15].

The existence of a history of preeclampsia implies a relative risk (RR) of 3.30 (95% CI: 1.672 - 6.513), $P < 0.05$ for the development of CKD, a value very similar to those found in a previous study with an RR of 4.77 (CI 95%: 3.88 - 5.86) [15]. These results suggest that attention should be given to the history of preeclampsia to provide timely nephrological follow-up in this population.

The present study described that the average time to present CKD in patients with preeclampsia was 3.95 years, with a

lower limit of 3.21 years and an upper limit of 4.7 years; these data slightly differ from those found in Villarreal [6].

To strengthen the finding of the risk of a history of PE in the development of CKD, a multivariate logistic regression analysis was carried out, where all those variables that turned out to have statistical significance were included, finding PE as the only predictor of risk in the development of CKD. Development of CKD with a B value of 1.27; $P = 0.001$ (95% CI 1.689 - 7.55) as a predictor of CKD, a finding that confirms the previous statistical analysis.

Conclusions

Preeclampsia is a factor associated with CKD; this knowledge can be used to remind health personnel of the implications of preeclampsia in the health of women of childbearing age in the short and long term and the need to implement prevention and control strategies for CKD. The prevalence of CKD in patients with a history of PE was 17.41%, a value comparable to the prevalence in other studies. The studied population that developed CKD corresponds to a young population; in this regard, the literature identifies 40 years as the average age, a group considered as a young adult, a scenario that can be considered critical due to the social repercussions if it is assumed that women represent 50% of the world population. The average time for the appearance of CKD between the history of PE and the appearance of any form of CKD was 3.95 years; with this study, it is suggested that at least a subset of women with previous data of preeclampsia need clinical follow-up for screening of kidney disease in the years immediately after pregnancy.

Abbreviations

CKD: chronic kidney disease.
PE: preeclampsia.
RR: relative risk.
OR: odds ratio.

Supplementary information

Supplementary materials have not been declared.



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Does not apply.

Author contributions

Norlys Margoth Fontalvo Díaz: Conceptualization, Data Curation, Formal Analysis, Fundraising, Research, Methodology, Project Management, Resources, Software, Writing – original draft.

Boris Marcelo Torres Zavala: Conceptualization, supervision, validation, visualization, and writing: review and editing.

Jorge Washing-ton Vélez Páez: Methodology, validation, supervision, writing: Review and editing.

All authors read and approved the final version of the manuscript.

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The authors provided research expenses.

Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available from the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

This study was approved by the bioethics committee (CEISH) of the Hospital Carlos Andrade Marín.

Consent to publication

It does not apply when images or photographs of the physical examination, X-rays/tomographies/MRIs of patients are not published.

Conflicts of interest

The authors report having no conflicts of interest.

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